DOCKET NO.: DIBIS-0003US (Counsel Docket No. 10310) **PATENT**

IN THE SPECIFICATION:

Marked Up Version. All instructions refer to the specification as filed:

Please delete the paragraph on page 1 lines 5 to 7 and replace it with the following:

STATEMENT OF GOVERNMENT SUPPORT

This invention was made with United States Government support under DARPA/SPO contract ~~BAA00-09~~ 4400044016. The United States Government ~~may have~~ has certain rights in the invention.

Please delete the paragraph on page 15 lines 14 to 27 and replace it with the following:

It is advantageous to design the "intelligent primers" to be as universal as possible to minimize the number of primers which need to be synthesized, and to allow detection of multiple species using a single pair of primers. These primer pairs can be used to amplify variable regions in these species. Because any variation (due to codon wobble in the 3rd position) in these conserved regions among species is likely to occur in the third position of a DNA triplet, oligonucleotide primers can be designed such that the nucleotide corresponding to this position is a base which can bind to more than one nucleotide, referred to herein as a "universal base." For example, under this "wobble" pairing, inosine (I) binds to U, C or A; guanine (G) binds to U or C, and uridine (U) binds to U or C. Other examples of universal bases include nitroindoles such as 5-nitroindole or 3-nitropyrrole (Loakes *et al.*, *Nucleosides and Nucleotides*, 1995, *14*, 1001-1003), the degenerate nucleotides dP or dK (Hill *et al.*), an acyclic nucleoside analog containing 5-nitroindazole (Van Aerschot *et al.*, *Nucleosides and Nucleotides*, 1995, *14*, 1053-1056) or the purine analog ~~1-(2-deoxy-β-D-ribofuranosyl)-imidazole-4-carboxamide~~ 1-(2-deoxy-beta-D-ribofuranosyl)-imidazole-4-carboxamide (Sala *et al.*, *Nucl. Acids Res.*, 1996, *24*, 3302-3306).

Please delete the paragraph on page 29, lines 5 to 6 and replace it with the following:

~~Table 4~~ Table 5 shows the expected molecular weight and base composition of region 16S_1100-1188 in *Mycobacterium avium* and *Streptomyces sp.*

Please delete the paragraph on page 29, lines 9-12 and replace it with the following:

~~Table 5~~ Table 6 shows base composition (single strand) results for 16S_1100-1188 primer amplification reactions from different species of bacteria. Species which are repeated in the table (e.g., *Clostridium botulinum*) are different strains which have different base compositions in the 16S_1100-1188 region.

Please delete the paragraph that begins on page 30 at line 2 and continues to page 31 at line 3, and replace it with the following:

The same organism having different base compositions are different strains. Groups of organisms which are in bold ~~highlighted or in italics~~ have the same base compositions in the amplified region. Some of these organisms can be distinguished using multiple primers. For example, *Bacillus anthracis* can be distinguished from *Bacillus cereus* and *Bacillus thuringiensis* using the primer 16S_971-1062 (Table 7 ~~Table 6~~). Other primer pairs which produce unique base composition signatures are shown in Table 7 ~~Table 6~~ (bold). Clusters containing very similar threat and ubiquitous non-threat organisms (e.g. *anthracis* cluster) are distinguished at high resolution with focused sets of primer pairs. The known biowarfare agents in Table 7 ~~Table 6~~ are *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis* and *Rickettsia prowazekii*.